ECT: It works, but at what cost?

A 30-year-old woman mired in a "catatonic stupor" received four electroconvulsive therapy (ECT) treatments. The therapy — which primarily consists of applying an electric current to one or both sides of the head — helped bring her out of the stupor. But following the treatments the woman experienced intense, grand mal seizures once or twice a week and had to be given anticonvulsive drugs.

The above example illustrates scientific and ethical dilemmas that continue to surround ECT. The use and known effects of electroconvulsive therapy are detailed in a newly released report by a task force of the American Psychiatric Association. "We are cognizant that some may view this report as self-serving because it has been assembled by an APA committee which comprises mostly APA members," concede the task force members. Having acknowledged that, the group explains that it surveyed about 3,000 APA members concerning their experiences and attitudes about the procedure. Psychiatrists who use ECT report that nearly eight of 10 patients who receive the treatment suffer from major depression and that most of the others are diagnosed as schizophrenics.

Those reports, plus a survey of various studies on ECT outcomes, reflect the general impression that electric shock is helpful in severe depression, particularly in cases where drugs have failed to alleviate symptoms. Responding psychiatrists said 88 percent of their patients were at least moderately satisfied with the results. The procedure's effect on schizophrenia, however, remains unknown, the report says.

Also unknown, though, are the exact mechanisms involved in running an electric current into the brain. The researchers attribute the "therapeutic process" in depression to the "biochemical events which accompany or result from seizures," which are intentionally triggered by the shocks.

But until more is known about the nature of such biochemical changes, ECT remains associated with "adverse effects," including memory loss, continuing seizures, cardiac dysrhythmias and psychological fear of the treatment itself. Some temporary memory loss is considered relatively common among ECT patients, particularly those who receive ECT on both sides of the head. However, the survey reveals that 27 percent of the patients experience *permanent* memory loss for the period of their ECT course (which usually involves several shock administrations over a period of time), and 15 percent have permanent memory loss for what occurred just prior to their treatment.

"We cannot be cavalier about ... memory dysfunctions," says Task Force leader Fred H. Frankel of Harvard University and Beth Israel Hospital in Boston. Some patients still complain of memory loss six to nine months after ECT, he says. The researchers have observed that placing both electrodes over the right brain hemisphere of right-handed patients appears to produce less memory loss than does bilateral ECT.

In weighing the advantages against the risks, the task force concludes that "ECT is an effective treatment" in cases of severe depression in which the risk of suicide is high, when the patient is not eating or drinking adequately or when drug and other therapy is inappropriate. The technique may also be used in severe psychoses if the patient is dangerous and drugs are inappropriate, and in cases of severe catatonia or severe mania. However, the researchers stress that "ECT should not be used solely to control symptoms or violent behavior."

They further note that the precautions taken and medical advances associated with ECT in the 1970s make it a "vastly different" procedure from the electroshock techniques "described over the past 30 years.... The status of ECT today is similar to that of psychotropic drugs in 1957-1962." Finally, they discourage the use of the term "shock" to describe the procedure and recommend "convulsive therapy" and "ECT" — "until a better name is formulated." □

HEW restricts research on prisoners, others

Department of Health, Education and Welfare Secretary Joseph A. Califano Jr. is temporarily prohibiting the use of HEW funds for psychosurgery on prisoners, children, involuntary mental patients and legally incompetent patients. The restriction, a response to the report of the National Protection of Human Subjects of Biomedical and Behavioral Research (SN: 5/14/77, p. 314), is in effect until HEW issues proposed regulations "in the near future," Califano says.

At the same time, Califano issued new regulations to severely restrict participation of prisoners in other types of HEW-funded research. The new rules *permit* "minimal risk" studies of possible causes, effects and processes of incarceration; studies of prisons as institutional, incarcerating structures; research — approved by Califano on a case-by-case basis — on social and psychological problems such as alcoholism, drug addiction and sexual assaults; medical studies, including vaccine trials, on diseases that are more prevalent in prisons than elsewhere (such as hepatitis); research "which has the intent and reasonable probability of improving the health or well-being of the subject." Studies requiring control groups, for example, could proceed only after the approval of the Secretary. □

Lasker awards: Brain and vaccine research

The Lasker awards, the most prestigious medical research awards in the United States (as well as recognition that often helps recipients go on to win a Nobel Prize), were announced this week. The awards go to scientists who have made outstanding contributions in bacterial antigen and bacterial vaccine research and in brain nerve and brain chemistry research.

The $15,000 Albert Lasker Clinical Medical Research Award is being shared by Michael Heidelberger of New York University School of Medicine, Robert Austrian of the University of Pennsylvania School of Medicine and Emil C. Gotschlich of Rockefeller University. Heidelberger established that the antigenic material enveloping the bacteria that cause pneumonia and meningococcus meningitis are sugars, and that when these sugars are purified and injected into a person, they raise antibodies against the bacteria from whence the sugars came. Austrian used this knowledge to develop a vaccine made of pneumonia sugar antigens. The vaccine was found to be highly effective in preventing bacterial pneumonia, a feat that experimental vaccines made from whole pneumonia bacteria could never claim (SN: 12/14/74, p. 381). The vaccine was then developed by a drug company and approved by the U.S. Food and Drug Administration in 1977 for commercial use.

Gotschlich used Heidelberger's discovery to develop a vaccine that contained sugar antigens from the meningococcus bacterium. This vaccine proved to be highly effective against meningococcal meningitis (SN: 12/14/77, p. 28), and it has been used routinely since 1971 in military training centers. Meningococcal meningitis is a disease that invades the central nervous system and that can lead to neurological damage and death.

The $15,000 Albert Lasker Basic Medical Research Award is being shared by Solomon H. Snyder of Johns Hopkins University School of Medicine, Hans W. Kosterlitz of the University of Aberdeen, Scotland, and John Hughes of the Imperial College of Science and Technology in London. During the early 1970s, Snyder and his colleagues identified, and then mapped, nerve membranes that bind opiate drugs. In 1975 Kosterlitz and Hughes (who were both at the University of Aberdeen at that time) identified two peptides naturally present in the brain that bind to the nerve receptors discovered by Snyder and his coworkers. These peptides, named enkephalins, turned out to be the brain's own natural "morphine," or pain-relieving chemicals, dramatically opening both the pain research field (SN: 10/14/78, p. 266) and the

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brain protein psychopharmacology field (see p. 374).

A $15,000 Albert Lasker Special Public Service Award is being shared by Elliot L. Richardson, former secretary of the Department of Health, Education and Welfare, and Theodore Cooper, former director of the National Heart, Lung and Blood Institute, for the massive campaign they launched to make the American public aware of the dangers of high blood pressure and of the need to seek treatment for it (SN: 12/11/76, p. 377). □

Lowering the sites on ozone

The problem with ozone is that no one knows how much of a problem it is. Chemicals such as methyl chloroform and fluorocarbons can thin the ozone layer at high altitudes, skew the ozone distribution and, as a result, change the way heat is conducted through the atmosphere. But major questions remain about the amount of ozone damage, about ozone's natural resilience and about the effects of ozone depletion on health and climate. A report expected early next year from the National Academy of Sciences will address some of these questions.

Part of the problem is the lack of good measurements. For example, Don Heath of Goddard Space Flight Center recently said that measurements from the Nimbus 4 satellite indicate only about half the ozone depletion found by ground based stations. However, he pointed out, the discrepancy could be cyclic, short- or long-term, natural or man-made. Only more measurements, like those to come from the Nimbus 7, will tell.

Most ozone studies are limited to the stratosphere, the layer 15 to 30 kilometers above the earth. That's another part of the problem, Jack Fishman of Colorado State University said last week at a meeting in Gatlinburg, Tenn., sponsored by the Council for the Advancement of Science Writing. Atmospheric scientists, he suggests, should lower their sites to the troposphere, the layer 8 to 15 km above.

According to Fishman, the troposphere may be a significant and overlooked source of ozone production from carbon monoxide and nitric oxide. If he is right, he says, then increases in CO and NO from the use of fossil fuels may raise the amount of ozone level in the lower atmosphere and aggravate the problems caused by thinning in the upper layers. Traditional theory says ozone is produced in the stratosphere, carried into the troposphere and destroyed near the ground; 90 percent exists in the stratosphere, 10 percent in the troposphere. Fishman says, "There is strong evidence that at least a considerable portion [of the 10 percent] in the troposphere is produced *in situ*."

More ozone exists in the northern hemisphere troposphere than in the southern hemisphere troposphere. But because more ozone is destroyed over land than over sea, more ozone is also destroyed in the northern hemisphere. Therefore, there must be a greater source of ozone in the north. This extra ozone has been attributed to more weather activity in the north, which carries more stratospheric ozone downward. But when Fishman and coworker Paul Crutzen examined the meteorological activities that might transport ozone into the lower atmosphere, they found no significant differences between the two hemispheres. The "reasonable" conclusion, Fishman says, is that the difference results from photochemical reactions in the troposphere.

Earlier work showed that OH is produced by the destruction of ozone near the ground. However, Fishman notes, OH also reacts with CO and NO to produce ozone. In the troposphere, he says, this series of competing reactions is normally in balance, but the heavier industrialization in the northern hemisphere may have provided enough CO and NO to tip the scale. Tropospheric measurements of ozone, NO and CO and comparisons of their distributions in the "pre-industrial" southern hemisphere and in the northern hemisphere will test his theory, he says. □

Natural prevention of genetic defects

It's hard to believe that in only a few years the technique of amniocentesis — the withdrawal of amniotic fluid from the womb of a pregnant woman to analyze fetal cells for genetic defects — has changed from a highly experimental diagnostic technique into a widely used one. Approximately 20,000 American women now take advantage of amniocentesis annually. What's more, the technique has come full circle and is now being used as a come full circle and is now being used as a research tool.

Geneticists have long known that powerful natural selective forces are at work to bring only healthy babies into the world. One-fourth of one-month-old human fetuses will be spontaneously aborted or miscarried because they are not genetically sound. Now Ernest B. Hook of the New York State Birth Defects Institute at Albany Medical College has analyzed results of amniocentesis tests and learned that such selective forces work well beyond the first three months of pregnancy, which was not previously thought to be the case, and they work for such serious genetic diseases as Down's syndrome (mongolism). Hook's work, reported in the Nov. 9 NEW ENGLAND JOURNAL OF MEDICINE, also examines the belief that women older than 40 years of age are especially likely to have a Down's child.

There had been some previous hints that miscarriages among Down's syndrome fetuses after the early part of pregnancy are rather common. So Hook decided to see whether this is in fact the case. He contacted the 149 prenatal diagnosis centers listed by the National Foundation-March of Dimes and asked them whether they had any cases on file of women having had fetuses diagnosed by amniocentesis for Down's syndrome and opting to have the child rather than have a therapeutic abortion. Hook also requested the outcomes of such pregnancies.

All but 15 of the 149 centers replied and reported, in total, 21 such cases. Of those 21 fetuses, Hook found, five had ended in miscarriage after amniocentesis had been performed, that is, during the latter half of pregnancy. This comes to a 24 percent chance of a spontaneous miscarriage during the latter half of pregnancy for a Down's fetus, versus a risk of only 3.5 percent for healthy fetuses (a figure previously obtained from amniocentesis test results). In other words, after the middle of pregnancy, there is about a sixfold higher risk of spontaneous death for a Down's fetus than for a healthy fetus, suggesting that Mother Nature continues to exert strong pressure even later in pregnancy to eliminate defective fetuses.

But perhaps the most valuable aspect of Hook's findings, says Godfrey P. Oakley Jr. of the Center for Disease Control in Atlanta in an accompanying NEJM editorial, is that it calls into question the widely held belief that women older than age 40 are at an excessively high risk of having a child with Down's syndrome. In other words, women older than 40 may be more likely than younger women to conceive a child with the syndrome, but it's quite possible that Down's fetuses conceived by older women may be even more subject to miscarriage throughout pregnancy than Down's fetuses conceived by younger women. If that is indeed the case, then women older than 40 would be no more at risk of giving birth to a Down's syndrome child than would younger women. The pregnancy outcomes of women past the age of 40 who have had amniocentesis for Down's syndrome, Oakley advises, should now be used to test this possibility. □

Death of a baby mammoth

Dima, the well-preserved mammoth discovered in Siberia (SN: 3/18/78, p. 167), died of blood poisoning approximately 44,000 years ago. That is the autopsy report just announced by the Tass news agency. "The mammoth died of blood infection," Tass said. "When he was still alive something hit his leg in two places and during his last hours of life he stopped eating." Soon after his death, the animal was buried by a mud flood. According to Tass, geologists had been unaware such flooding took place in northern Siberia. □